Acute retroviral syndrome

Javier R. Lama[a], *Rachel A. Bender Ignacio*[b,c] *and Ann Duerr*[c]

Purpose of review
To review the most important recent literature on the definition, epidemiology, clinical presentation, pathogenesis and treatment of the acute retroviral syndrome (ARS), a constellation of nonspecific symptoms and transient illness occuring in at least 50% of persons shortly after HIV acquisition. ARS is driven by initial rapid HIV viral replication and dissemination after acquisition, followed by immune activation and massive systemic inflammation. A more detailed understanding of ARS is important for the implementation of early detection efforts, treatment and public health strategies to control HIV.

Recent findings
Recent research has provided deeper insights into ARS. Key findings include associations of ARS with heightened immune activation and elevated levels of IFN-γ and multiple other cytokines, particularly IP-10, as well as with higher viral load and more severe $CD4^+$ depletion during acute infection. These negative impacts can be mitigated by early antiretroviral therapy initiation and long-term outcomes are generally similar in treated individuals with or without ARS.

Summary
Current findings underscore the importance of early detection and intervention in ARS to mitigate long-term health impacts and inform the development of targeted therapeutic strategies.

Keywords
acute HIV infection, acute retroviral syndrome, HIV diagnosis, HIV prevention, HIV treatment

INTRODUCTION

Acute HIV infection (AHI), the earliest stage following HIV acquistion, often defined as the period between the detection of HIV RNA in the plasma and the development of anti-HIV-antibodies [1], can occur asymptomatically or can cause an acute retroviral syndrome (ARS). ARS, a constellation of nonspecific symptoms and transient illness, is estimated to occur in at least 50% of persons shortly after HIV acquisition [1]. It is driven by initial rapid viral replication and dissemination after acquisition, followed by immune activation and massive systemic inflammation. Early recognition of ARS could provide a unique opportunity for interventions during AHI, including testing for HIV RNA and rapid treatment initiation, which have been shown to improve long-term individual clinical outcomes [2–4].

Immediately after acquisition, as HIV is replicating in the mucosa, submucosa (if acquisition occurred by sexual exposure) and draining lymphoid tissues, the virus cannot be detected in plasma, a period defined as the eclipse phase, which generally lasts 7–21 days [5]. What follows is the orderly appearance of viral and host markers of infection in plasma which serve as the basis for diagnosis and staging of HIV [6], known as Fiebig staging. This has been widely adopted in studies assessing the benefits of treatment initiation during AHI [7▪▪]. However, Fiebig staging is rarely used in contemporary clinical practice, as some of the required laboratory tests are no longer a part of HIV diagnostic algorithms.

EPIDEMIOLOGY

Estimates of the frequency of ARS vary widely; several factors contribute to this [8,9▪,10]. First, because the signs and symptoms of ARS are nonspecific and because the onset of ARS typically occurs prior to development of the anti-HIV antibody responses detected by routine serologic tests, ARS often goes

[a]Asociacion Civil Impacta Salud y Educación, Lima, Peru, [b]University of Washington and [c]Fred Hutchinson Cancer Center, Seattle, Washington, USA

Correspondence to Javier R. Lama, MD, MPH, Asociacion Civil Impacta Salud y Educacion, Av. Almirante Miguel Grau 1010, Lima 15063, Peru. Tel: +51 99752 0405; e-mal: jrlama@impactaperu.org

Curr Opin HIV AIDS 2025, 20:186–192

DOI:10.1097/COH.0000000000000933

Copyright © 2025 Wolters Kluwer Health, Inc. All rights reserved.

SHOUT
SHARE
IT

KEY POINTS

- Acute retroviral syndrome (ARS) represents a critical window of opportunity for HIV diagnosis and intervention to prevent further clinical and immunological impairment, as well as prevent onward transmission.
- Enhanced awareness among populations at risk and healthcare providers, as well as routine ('opt-out') HIV testing in healthcare settings, can lead to more consistent detection of ARS.
- Early diagnosis and antiretroviral therapy initiation during ARS limit the viral reservoir and are expected to improve long-term outcomes and reduce the likelihood opportunistic infections and non-AIDS related illness. In addition, treatment initiation during this period of peak viremia dramatically reduces the likelihood of onward HIV transmission.
- Characterizing the immunopathogenesis of ARS, by identifying better tools for early diagnosis and prediction of long-term outcomes based on acute-phase immune response, will support the development of novel therapeutic interventions.

undiagnosed. Second, because HIV diagnosis typically occurs months to years after acquisition, accurate reporting of whether a person previously experienced ARS and, if so, what symptoms were present, is subject to recall bias. Third, individuals with more severe, clinically apparent ARS are more likely to come to medical attention and to be diagnosed with HIV-associated ARS, and so mild ARS is often not identified by the people with HIV or providers. Finally, definitions of ARS vary with some studies requiring the presence of multiple signs and symptoms and others considering a single sign or symptom as ARS. Thus, prospective studies which closely monitor at-risk populations for incident HIV with well defined definitions of ARS are needed to minimize ascertainment and recall biases, and to allow more precise estimation of the numerator (ARS) and the denominator (people with recent HIV acquisition) (Fig. 1). Estimates from several such studies follow; *Sabes* and RV217 studies also collected data on prevalence of nonspecific ARS symptoms at study entry prior to HIV acquisition to allow comparison to those reported during AHI.

In the *Sabes* study conducted in Peru, 2109 men who have sex with men (MSM) and transgender women without HIV were followed monthly with HIV testing (serology and HIV RNA) and symptom history. Among 216 individuals diagnosed with incident HIV, 39% had no clinical manifestations of ARS, while 61% had documentation of at least one symptom or sign and 35% had three or more. Fig. 2 depicts the distribution of symptoms and signs observed among *Sabes* participants who described at least one. ARS findings were most common in those enrolled within a month of estimated dates of detectable infection (EDDI) and fever, pharyngitis and malaise were reported most often [9▪].

The RV217 study conducted among 2276 participants in Kenya, Uganda, Tanzania and Thailand with risk factors for HIV acquisition collected blood samples twice weekly and tested for HIV RNA to detect AHI [8]. Fifty participants with incident HIV detected prior to seroconversion were included in the analysis. While few, if any, signs or symptoms were reported prior to infection, 94% of participants reported one or more during the 'acute infection' period (from five visits before to five after peak viremia). However, at visits which included a physical examination, participants reported no symptoms and 50% of participants had neither symptoms nor signs. Signs and symptoms occurred most frequently at the study visit prior to (3–4 days before) peak viremia; fever was the most frequently reported symptom, although few participants were febrile on examination.

Participants from several key populations (serodifferent couples, sex workers and their clients, MSM, adolescents) in Kenya, Rwanda, Uganda, Zambia and South Africa were followed with monthly or quarterly testing for HIV, depending on the study site. Participants with incident HIV were invited to join IAVI Protocol C [11]. Data analysis was limited to 183 participants with incident HIV who were enrolled within 6 weeks of the estimated date of HIV acquisition. One or more ARS symptom was reported by 84% of participants with subtype A HIV compared to 60% of participants with subtype C or D.

In a preliminary analysis of the FRESH cohort, which follows young women in South Africa with twice-weekly monitoring for HIV RNA, 9/11 participants with acute HIV reported flu-like illness [10].

Although it used a different methodology, the RV254/SEARCH 010 study in Thailand provided data on a large number of participants with ARS. In this study, 430 participants with AHI diagnosed at routine HIV testing (seronegative with positive HIV NAAT test or positive for anti-HIV IgM but negative for anti-HIV IgG) were enrolled; 78% had ARS defined as the presence of three or more qualifying symptoms. ARS was least common (27%) among participants enrolled in Fiebig stage 1 (HIV RNA+, seronegative) and more frequent in later stages. Fever, fatigue, pharyngitis and headache were the most common symptoms [12].

In summary, unbiased assessment of ARS is more likely in studies with close prospective follow-up

Copyright © 2025 Wolters Kluwer Health, Inc. All rights reserved.

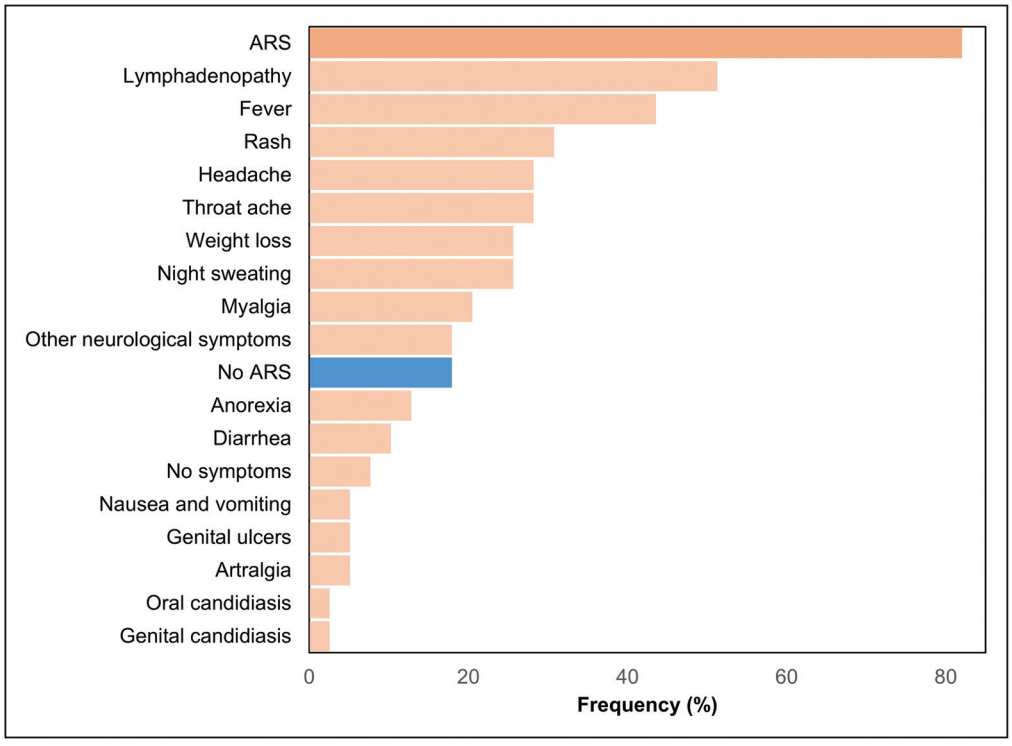

FIGURE 1. Acute retroviral syndrome among people very early diagnosed with and treated for HIV. Frequency of acute retroviral syndrome (ARS) and ARS signs and symptoms at the time of HIV diagnosis (Belgian Acute HIV Infection Cohort; $n = 39$). Adapted from [21▪].

with frequent HIV testing of at-risk participants. ARS is common in studies with this design, occurring in over half of participants in all studies, and up to 90% in several. Differences in prevalence and reported signs/symptoms likely arise due to differences in data collection method (self-report versus physician collected signs), location (country as well as HIV subtype) and Fiebig stage or estimated time since HIV acquisition. Table 1 summarizes the most relevant characteristics of assessed cohorts describing the occurrence of symptoms ans signs of ARS.

CLINICAL PRESENTATION

Characterization of ARS, like prevalence estimates, is often limited by ascertainment bias due to its nonspecific nature and lack of recognition of its presentation. Symptoms, signs and laboratory abnormalities occurring in ARS are secondary to an inflammatory response to HIV. ARS can present in multiple ways and symptoms are usually mild-to-moderate and self-limited. However, the inflammatory processes associated with AHI can sometimes trigger a cytokine storm or cytokine release syndrome (CRS, characterized by fever, splenomegaly and cytopenias) or hemophagocytic lymphohistiocytosis that may be under recognized [13]. Unlike other cytokine release scenarios, ARS-associated CRS generally responds well to targeted therapy of the underlying condition- in this case antiretroviral therapy (ART) initiation.

ARS encompasses a range of clinical conditions, from mild flu-like disease to severe multisystem dysfunction, and unusual clinical presentations are frequent [14]. The most common clinical manifestations occur at the peak of viremia, with symptoms typically resolving within 14 days [8]. The description of symptoms and signs varies, because outside of highly surveilled populations, most HIV diagnoses are made months or years after acquisition and recall of distant nonspecific symptoms is subject to bias. Overall, the most frequently reported clinical manifestations are fever, headache, malaise, tachycardia, other head and neck symptoms, and lymphadenopathy [8]. Fatigue, myalgia, weight loss, night sweats, skin rash, pharyngitis, gastro-intestinal symptoms, aseptic meningitis and oral or genital ulcers have also been reported [1]. Some symptoms have better discriminatory ability for ARS than others. For example, latent class analysis was used to identify which symptoms were most strongly associated with true ARS; myalgia had the best discriminatory ability, while fever, cough and skin rash poorly differentiated those with and without true ARS and associated biomarker changes

Copyright © 2025 Wolters Kluwer Health, Inc. All rights reserved.

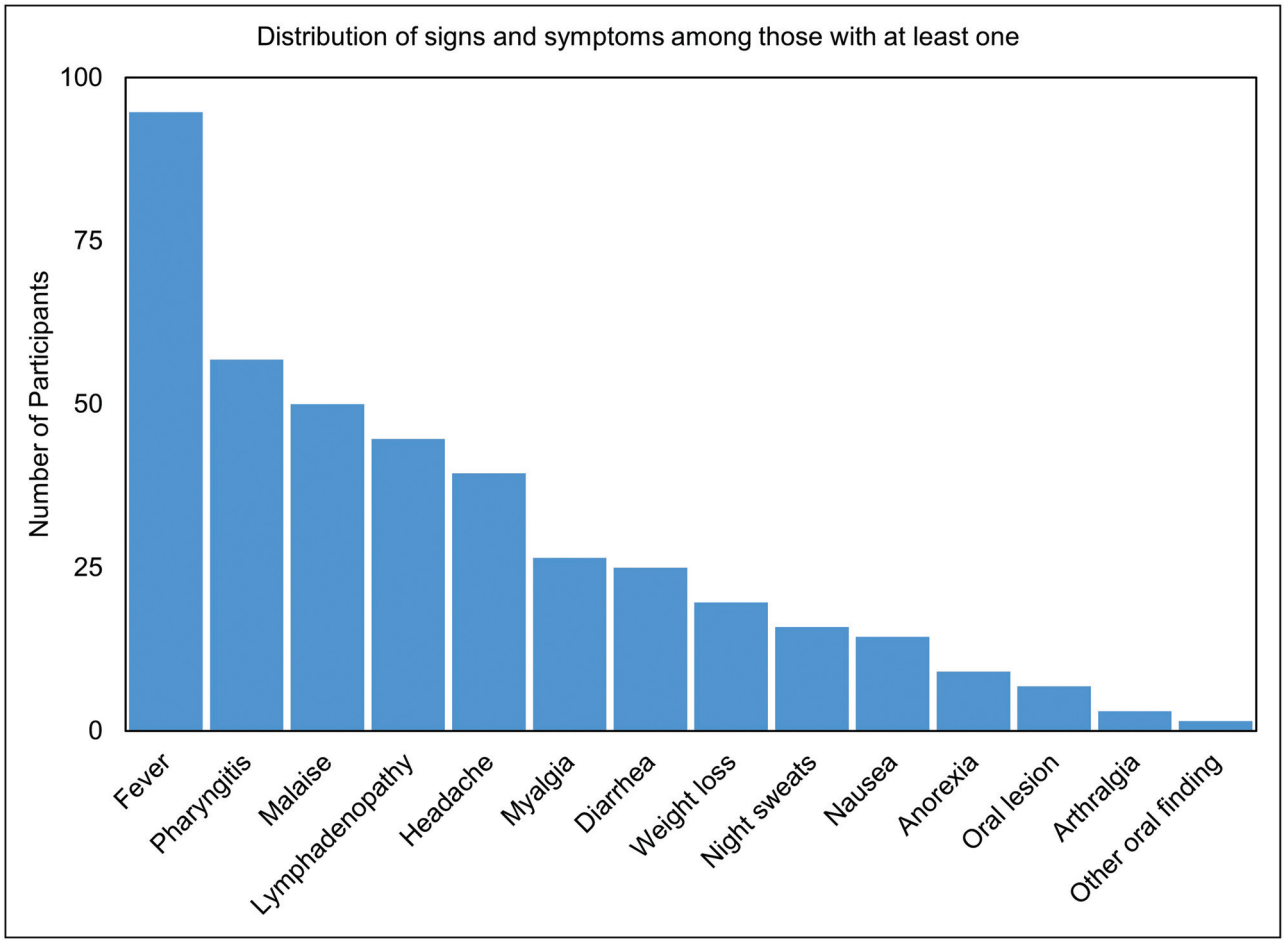

FIGURE 2. Signs and Symptoms of Acute Retroviral Syndrome. Frequency of signs and symptoms of acute retroviral syndrome among 132 out of 216 MSM and transgender women diagnosed with incident HIV (*Sabes* Study). Adapted from [9▪].

in one multinational cohort [15]. Leukopenia, thrombocytopenia and elevation of liver enzymes are present in one third to one half of cases [16]. Rare cases of AHI causing severe acute hepatitis have also been reported [8]. Opportunistic infections may also occur during AHI and are sometimes labeled as

Table 1. Most relevant data from cohorts assessed for the presence of symptoms and signs of acute retroviral syndrome

Study	Location	Number of participants	Prevalence of ARS (self-report of ≥1 finding)[a]	Most common signs	Most common symptoms	References
Sabes	Peru	216	61%	Lymphadenopathy	Fever, pharyngitis, malaise	[9▪]
RV217	Kenya Uganda Tanzania Thailand	2276	94%	Tachycardia, lymphadenopathy, other head & neck findings	Fever, headache, malaise	[8]
IAVI Protocol C	Kenya Uganda Rwanda Zambia South Africa	183	Subtype A: 84% Subtype C or D: 60%		Fever, headache myalgia/arthralgia, fatigue	[11]
RV254/ SEARCH 010	Thailand	430	78% (≥3 signs or symptoms)	Weight loss, diarrhea, skin rash	Fever, fatigue, pharyngitis, headache	[12]

[a]Except for RV254/SEARCH 010 which reported results for ≥3 signs or symptoms.

Copyright © 2025 Wolters Kluwer Health, Inc. All rights reserved.

'atypical ARS' symptomatology, including cytomegalovirus or herpes simplex hepatitis, CMV gastritis or colitis, candida mucocutaneous infections, multidermatome herpes zoster and encephalitis [4,14]. Persons with atypical symptoms in the absence of typical ARS are more likely to have delayed HIV diagnosis and a higher rate of hospitalization [14].

Clinical presentation has been reported to vary between populations, although the importance of many of these associations is unclear. For example, in a multicountry study wherein HIV subtype varied geographically, ARS symptoms were more frequently reported in individuals with HIV subtype A infection compared to individuals with subtype C and D [11]. In the RV217 study including participants from Kenya, Uganda, Tanzania and Thailand, lymphadenopathy was observed more frequently in participants in Thailand than in East Africa [8]. HLA type was reported not to be associated with ARS in the study of 183 IAVI Protocol C participants published in 2017 [11]. In a subsequent publication considering a more narrowly defined subgroup of 72 participants from the same study, significant protection was associated with HLA A*23 (adjusted Odds Ratio = 0.10, $P = 0.009$) but not with the other HLA-A ($N = 15$), HLA-B ($N = 12$), HLA-C ($N = 22$) molecules or KIR genes ($N = 22$) examined [8,17].

The occurrence of a retroviral rebound syndrome (RRS) mimicking ARS has been also described among individuals who interrupt ART, although it appears to occur rarely, a literature review conducted in 2021 reported only 19 cases [18]. In an ACTG study including analytic treatment interruption, 3/33 (9%) participants who started ART in chronic HIV but none (0/12) of early-treated individuals experienced RRS [19].

PATHOGENESIS

ARS is associated with a strong immune reaction during acute HIV. While all persons with primary HIV experience well documented changes in immune cell dynamics and soluble biomarkers, several studies have shown that the presence and degree of symptoms during AHI are associated with more severe immunopathogenesis [20]. In a cohort of persons in Sweden and East Africa with hyperacute HIV, compared to persons without ARS, those with ARS had higher levels of 18 soluble biomarkers, with differences in IP-10 being the most prominent. Persons with ARS also had higher levels of interferon-gamma, granulocyte-macrophage colony stimulating factor, IL-10, IL-13, IL-15, flt-1 and eotaxin-3 [15].

In the *Sabes* study conducted in Peru, higher IP-10 levels were also most strongly associated with ARS symptomatology, with a 0.7 $\log_{10}$ difference between those with 0, 1-2 or 3 or more ARS findings, or a 0.5 $\log_{10}$ increase across ARS categories when adjusted by time since estimated HIV acquisition [9▪]. In unadjusted analysis, there was also a trend towards positive associations of MCP-1, IL-23, interferon gamma levels with increasing numbers of ARS symptoms/signs, and a negative association with TNF-β. Higher number of ARS findings was also associated with lower $CD4^+$ nadir and higher peak viral load during acute infection. Among participants who maintained viral load suppression on ART, there was no association between ARS and $CD4^+$ or $CD8^+$ cell count or CD4/CD8 ratio after 4 years.

In the RV254/SEARCH study in Thailand, participants with ARS also had higher levels of HIV RNA in the blood, colon and cerebral spinal fluid, and higher levels of HIV DNA. As in the *Sabes* study, participants with ARS had more $CD4^+$ depletion in blood (and colon) and lower CD4/CD8 ratio; the differences between groups resolved at 2 years on ART [12]. However, 2 two years, TNF-α and IL-6 remained elevated in those who experienced ARS compared to those who did not, although no associations with IP-10 were found at baseline or during ART in this cohort.

A smaller study in Belgium found longitudinal elevations in IL-6, IL-1RA and IP-10 in persons with ARS versus those with asymptomatic acute HIV; CXCL-1 and IL-7 were higher in those without ARS or without HIV compared to those with ARS. This study also found that higher levels of plasma markers of inflammation prior to HIV acquisition predicted ARS [21▪]. In addition, in a study of untreated hyperacute HIV among African women, participants with faster replicating (more virulent) HIV had the highest levels of IP-10 and TNF [20].

The Zurich Primary HIV Infection Study (ZPHIS) developed an ARS severity score (ARSS), which, after adjustment for EDDI, was associated with higher baseline viral load load and lower $CD4^+$ cell count [22]. In contrast to the *Sabes* study, these investigators found no association between ARSS and time to viral suppression [9▪]. ZPHIS evaluated associations with HLA type and found no association between ARSS and human genetics.

TREATMENT

Initiating ART during ARS represents a shift in HIV management, emphasizing the importance of immediate action after diagnosis. ART should be initiated as soon as possible, even in the absence of results from resistance testing. Early intervention not only benefits the individual by preserving their health but also contributes to broader public health goals of controlling and eventually eradicating HIV

Copyright © 2025 Wolters Kluwer Health, Inc. All rights reserved.

[23]. An overview of the key benefits on ARS is presented as follows.

The *Sabes* study, which was conducted in Peru prior to universal ART guidelines, included randomization to time of ART initiation. Persons who started ART during acute and early HIV infection (AEHI) versus 6 months later had fewer symptoms overall during their early HIV course, specifically fewer reports of pharyngitis, headache and fever, all likely part of ARS [4]. In addition to overall symptoms, persons who started ART immediately during AEHI were less likely to experience opportunistic infections, which generally occur in late HIV, but can occur during the drop in $CD4^+$ cell count during acute infection. Infections seen in those not on ART during the acute HIV in *Sabes* included herpes zoster (shingles), oral candidiasis, oral hairy leukoplakia and upper and lower respiratory tract infections, including extrapulmonary tuberculosis. ARS symptom relief, including reducing severity and duration, should be theoretically achieved through early ART initiation [24].

Although persons with ARS are more likely to experience a lower $CD4^+$ cell count nadir and prolonged time to suppress viremia than those with few or no ARS symptoms, these effects were mitigated in those who started ART immediately in a follow-on analysis of the *Sabes* study [9▪].

Notably, studies evaluating the impact of ART on ARS symptoms and pathogenesis were predominately prior to 2016 when the WHO suggested treating all people with HIV at the time of diagnosis, and therefore were also predominately using nonintegrase inhibitor-based regimens. With the more rapid decline in viral load after initiation of an integrase-based regimen than prior ART anchors, the impact of treatment on ARS resolution might be stronger (or perhaps more rapid) [25]. Additionally, use of an integrase-based regimen could improve neurologic symptoms more effectively than efavirenz-based regimens, which could themselves contribute to neuropsychiatric symptomology [26].

Early suppression of viral load reduces reservoir formation, minimizes immune system damage and improves long-term outcomes. Very early ART initiation during the time when ARS is most likely to occur is associated with faster rates of decay of the latent HIV reservoir and lower levels of HIV DNA in PBMC, providing a window of opportunity for curing HIV [27–29].

ART initiation during acute HIV also preserves immune system function by safeguarding $CD4^+$ T cells [30,31], and limits immune activation [4,32], although these benefits will likely accrue to all those who initiate ART early whether they have ARS or not.

Because maximal ARS symptomatology roughly coincides with the peak of viremia during AHI, ART initiation during ARS has the potential to reduce onward HIV transmission to sexual partners [33,34], especially if viral load can be rapidly reduced to undetectable (Undetectable = Untransmittable).

While the benefits of treating ARS are significant, there are also potential challenges associated with initiating treatment during this early stage, including difficulty confirming HIV diagnosis during ARS, as symptoms are nonspecific and serologic assays will likely be negative, and the need to assure adequate patient counseling and linkage to the HIV care continuum.

The benefits of early ART initiation have now been amply demonstrated as a means of improving short-term and long-term clinical and immunopathologic outcomes, as well as providing population-level benefit by reducing onward HIV transmission. While ARS is not present in all persons with AHI, the majority of persons experience symptoms, such that public and clinician education around recognition of ARS could provide an adjunct to efforts to assure timely ART initiation during acute and early HIV.

CONCLUSION

ARS serves as both a clinical challenge and an opportunity. Addressing gaps in its diagnosis and treatment will not only improve individual patient outcomes but also contribute significantly to controlling the global HIV epidemic. Ongoing research and collaboration between clinicians, researchers and public health officials are essential to fully address this critical phase following HIV acquistion.

Acknowledgements

None.

This manuscript has been seen, reviewed and approved by all contributing authors.

Financial support and sponsorship

None.

Conflicts of interest

The authors do not have any conflict of interest to report.

REFERENCES AND RECOMMENDED READING

Papers of particular interest, published within the annual period of review, have been highlighted as:

- ▪ of special interest
- ▪▪ of outstanding interest

1. Henn A, Flateau C, Gallien S. Primary HIV infection: clinical presentation, testing, and treatment. Curr Infect Dis Rep 2017; 19:37.

Copyright © 2025 Wolters Kluwer Health, Inc. All rights reserved.

2. Crowell TA, Phanuphak N, Pinyakorn S, *et al.* Virologic failure is uncommon after treatment initiation during acute HIV infection. AIDS 2016; 30: 1943–1950.
3. Hogan CM, Degruttola V, Sun X, *et al.* The setpoint study (ACTG A5217): effect of immediate versus deferred antiretroviral therapy on virologic set point in recently HIV-1-infected individuals. J Infect Dis 2012; 205:87–96.
4. Lama JR, Ignacio RAB, Alfaro R, *et al.* Clinical and immunologic outcomes after immediate or deferred antiretroviral therapy initiation during primary human immunodeficiency virus infection: the Sabes randomized clinical study. Clin Infect Dis 2021; 72:1042–1050.
5. Cohen MS, Shaw GM, McMichael AJ, Haynes BF. Acute HIV-1 infection. N Engl J Med 2011; 364:1943–1954.
6. Fiebig EW, Wright DJ, Rawal BD, *et al.* Dynamics of HIV viremia and antibody seroconversion in plasma donors: implications for diagnosis and staging of primary HIV infection. AIDS 2003; 17:1871–1879.
7. ■■ De Clercq J, Rutsaert S, De Scheerder MA, *et al.* Benefits of antiretroviral therapy initiation during acute HIV infection. Acta Clin Belg 2022; 77:168–176.
This article conducts a review of acute HIV infection, including ARS, emphasizing in the individual and societal benefits of the early initiation of antiretroviral therapy in this period.
8. Robb ML, Eller LA, Kibuuka H, *et al.* Prospective study of acute HIV-1 infection in adults in East Africa and Thailand. N Engl J Med 2016; 374:2120–2130.
9. ■ Gabert R, Lama JR, Valdez R, *et al.* Acute retroviral syndrome is associated with lower CD4 + T cell nadir and delayed viral suppression, which are blunted by immediate antiretroviral therapy initiation. AIDS 2023; 37:1103–1108.
This study describes the frequence of signs and symptoms of ARS among MSM and transgender women diagnosed with incident HIV infection in Lima, Peru and their association with inmunological parameters, highligthing the benefits of the early initiation of antiretroviral therapy.
10. Walker KDAMTNB, editor. Fresh cohort; acute HIV-1 infection in cohort of high risk Hiv negative women in KZN South Africa. Conference on Retroviruses and Opportunistic Infections; 3–6 March 2014; Boston, MA.
11. Sanders EJ, Price MA, Karita E, *et al.* Differences in acute retroviral syndrome by HIV-1 subtype in a multicentre cohort study in Africa. AIDS 2017; 31:2541–2546.
12. Crowell TA, Colby DJ, Pinyakorn S, *et al.,* RV254/SEARCH010 Study Group. Acute retroviral syndrome is associated with high viral burden, CD4 depletion, and immune activation in systemic and tissue compartments. Clin Infect Dis 2018; 66:1540–1549.
13. Erdmann N, Heath SL. Cytokine storm syndrome as a manifestation of primary HIV infection. Adv Exp Med Biol 2024; 1448:269–274.
14. Braun DL, Kouyos RD, Balmer B, *et al.* Frequency and spectrum of unexpected clinical manifestations of primary HIV-1 infection. Clin Infect Dis 2015; 61:1013–1021.
15. Hassan AS, Hare J, Gounder K, *et al.* A stronger innate immune response during hyperacute human immunodeficiency virus type 1 (HIV-1) infection is associated with acute retroviral syndrome. Clin Infect Dis 2021; 73:832–841.
16. Sun HY, Chen MJ, Hung CC, *et al.* Clinical presentations and virologic characteristics of primary human immunodeficiency virus type-1 infection in a university hospital in Taiwan. J Microbiol Immunol Infect 2004; 37:271–275.
17. Lindquist L, Kilembe W, Karita E, *et al.* HLA-A∗23 is associated with lower odds of acute retroviral syndrome in Human Immunodeficiency Virus Type 1 infection: a multicenter sub-Saharan African study. Open Forum Infect Dis 2024; 11:ofae129.
18. Akagi Y, Tanaka K, Mawatari M, *et al.* Clinical characteristics of retroviral rebound syndrome: a case report and literature review. Intern Med 2023; 62:1089–1093.
19. Li JZ, Aga E, Bosch RJ, *et al.* Time to viral rebound after interruption of modern antiretroviral therapies. Clin Infect Dis 2022; 74:865–870.
20. Muema DM, Akilimali NA, Ndumnego OC, *et al.* Association between the cytokine storm, immune cell dynamics, and viral replicative capacity in hyperacute HIV infection. BMC Med 2020; 18:81.
21. ■ De Clercq J, De Scheerder MA, Mortier V, *et al.* Longitudinal patterns of inflammatory mediators after acute HIV infection correlate to intact and total reservoir. Front Immunol 2023; 14:1337316.
This manuscript reports the evolution of residual inflammatory mediators associated with acute HIV infection in Belgium highlighting that persistent pro-inflammatory profile observed in early ART-treated individuals is shaped during acute HIV infection and is intertwined with viral dynamics.
22. Braun DL, Kouyos R, Oberle C, *et al.* A novel Acute Retroviral Syndrome Severity Score predicts the key surrogate markers for HIV-1 disease progression. PLoS One 2014; 9:e114111.
23. Smith MK, Rutstein SE, Powers KA, *et al.* The detection and management of early HIV infection: a clinical and public health emergency. J Acquir Immune Defic Syndr 2013; 63 Suppl 2:S187–S199.
24. Fidler S, Fox J, Touloumi G, *et al.,* Collaboration C. Slower CD4 cell decline following cessation of a 3 month course of HAART in primary HIV infection: findings from an observational cohort. AIDS 2007; 21:1283–1291.
25. Brinkman K. Getting acute HIV infection under control. AIDS 2023; 37:1157–1158.
26. Sax PE, DeJesus E, Mills A, *et al.* Co-formulated elvitegravir, cobicistat, emtricitabine, and tenofovir versus co-formulated efavirenz, emtricitabine, and tenofovir for initial treatment of HIV-1 infection: a randomised, double-blind, phase 3 trial, analysis of results after 48 weeks. Lancet 2012; 379:2439–2448.
27. Hiner CR, Mueller AL, Su H, Goldstein H. Interventions during early infection: opening a window for an HIV cure? Viruses 2024; 16:1588.
28. Barbehenn A, Shi L, Shao J, *et al.* Rapid biphasic decay of intact and defective HIV DNA reservoir during acute treated HIV disease. Nat Commun 2024; 15:9966.
29. Massanella M, Ignacio RAB, Lama JR, *et al.* Long-term effects of early antiretroviral initiation on HIV reservoir markers: a longitudinal analysis of the MERLIN clinical study. Lancet Microbe 2021; 2:e198–e209.
30. Rinaldi S, Pallikkuth S, Cameron M, *et al.* Impact of early antiretroviral therapy initiation on HIV-specific CD4 and CD8 T cell function in perinatally infected children. J Immunol 2020; 204:540–549.
31. Garcia-Broncano P, Maddali S, Einkauf KB, *et al.* Early antiretroviral therapy in neonates with HIV-1 infection restricts viral reservoir size and induces a distinct innate immune profile. Sci Transl Med 2019; 11:eaax7350.
32. Suanzes P, Navarro J, Rando-Segura A, *et al.* Impact of very early antiretroviral therapy during acute HIV infection on long-term immunovirological outcomes. Int J Infect Dis 2023; 136:100–106.
33. Cohen MS, Chen YQ, McCauley M, *et al.* Antiretroviral therapy for the prevention of HIV-1 transmission. N Engl J Med 2016; 375:830–839.
34. Rodger AJ, Cambiano V, Bruun T, *et al.* Risk of HIV transmission through condomless sex in serodifferent gay couples with the HIV-positive partner taking suppressive antiretroviral therapy (PARTNER): final results of a multicentre, prospective, observational study. Lancet 2019; 393:2428–2438.

Copyright © 2025 Wolters Kluwer Health, Inc. All rights reserved.